AMENDMENTS TO THE CLAIMS

Please cancel claims 14-17, 19, 22-27, 29-39, 41, 42, 44-64, 66-89 and 91-96 without prejudice.

1. **(Original)** A chimeric nuclease comprising: (i) a DNA binding domain; (ii) a cleavage domain; and (iii) a nuclear localization signal.

2. **(Original)** The chimeric nuclease of claim 1, wherein the DNA binding domain binds to a recognition sequence comprising at least 6 designated nucleotides.

3. **(Original)** The chimeric nuclease of claim 1, wherein the DNA binding domain comprises at least one zinc finger domain.

4. **(Original)** The chimeric nuclease of claim 1, wherein the DNA binding domain comprises three or more zinc finger domains.

5. **(Original)** The chimeric nuclease of claim 1, wherein the cleavage domain comprises a cleavage domain of a type IIs restriction endonuclease.

6. **(Original)** The chimeric nuclease of claim 1, wherein the cleavage domain comprises a cleavage domain of a FokI restriction endonuclease.

7. **(Original)** The chimeric nuclease of claim 1, wherein the DNA binding domain comprises three zinc finger domains and binds to a recognition sequence comprising 9 designated nucleotides, and wherein the cleavage domain is a cleavage domain of a FokI restriction endonuclease.

8. **(Original)** A chimeric nuclease comprising:
(a) a cleavage domain; and
(b) a DNA binding domain comprising at least three zinc fingers,
wherein the DNA binding domain binds to a recognition sequence that occurs at a position in a mammalian genome within at least 500 base pairs of an allele that contributes to a genetic disorder, and wherein the recognition sequence comprises at least 9 nucleotides.

9. **(Original)** A complex comprising a first chimeric nuclease and a second chimeric nuclease, wherein the first chimeric nuclease comprises a cleavage domain and a DNA binding domain, and wherein the second chimeric nuclease comprises a cleavage domain and a DNA binding domain.

10. **(Original)** The complex of claim 9, wherein the first chimeric nuclease comprises a DNA binding domain that comprises at least three zinc finger domains and that recognizes a sequence comprising at least 9 designated nucleotides.

11. **(Original)** The complex of claim 10, wherein the second chimeric nuclease comprises a DNA binding domain that comprises at least three zinc finger domains and that recognizes a sequence comprising at least 9 designated nucleotides.

12. **(Original)** The complex of claim 9, wherein the first chimeric nuclease and/or the second chimeric nuclease further comprises a nuclear localization signal.

13. **(Original)** A nucleic acid encoding a chimeric nuclease, wherein the chimeric nuclease comprises: (i) a DNA binding domain; (ii) a cleavage domain; and (iii) a nuclear localization signal (NLS).

14-17. **(Canceled)**

18. **(Original)** A nucleic acid encoding a chimeric nuclease, the chimeric nuclease comprising:
(a) a cleavage domain; and
(b) a DNA binding domain comprising at least three zinc fingers,
wherein the DNA binding domain binds to a recognition sequence that occurs at a position in a mammalian genome within at least 500 base pairs of an allele that contributes to a genetic disorder, and wherein the recognition sequence comprises at least 9 nucleotides.

19. **(Canceled)**

20. **(Original)** A vector comprising
(a) a nucleic acid encoding a first chimeric nuclease; and
(b) a nucleic acid encoding a second chimeric nuclease,

wherein the second chimeric nuclease forms a heterodimer with said first chimeric nuclease.

21. **(Original)** A vector comprising:
(1) a nucleic acid encoding a chimeric nuclease that comprises: (i) a DNA binding domain; and (ii) a cleavage domain; and
(2) a nucleic acid comprising a repair substrate that comprises: (i) a nucleic acid sequence that is substantially identical to a region flanking a target sequence in chromosomal DNA; and (ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence.

22.-27. **(Canceled)**

28. **(Original)** A mammalian cell comprising: (a) a chimeric nuclease; and (b) a repair substrate, wherein the chimeric nuclease comprises:
(i) a DNA binding domain; and
(ii) a cleavage domain,
and wherein the repair substrate comprises:
(i) a nucleic acid sequence that is substantially identical to a region flanking a target sequence in chromosomal DNA; and
(ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence.

29.- 39. **(Canceled)**

40. **(Original)** A mammalian cell comprising a nucleic acid encoding a chimeric nuclease and a nucleic acid comprising a repair substrate, wherein the chimeric nuclease comprises:
(i) a DNA binding domain; and
(ii) a cleavage domain,
and wherein the repair substrate comprises:
(i) a nucleic acid sequence that is substantially identical to a region flanking a target sequence in chromosomal DNA; and
(ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence.

41. **(Canceled)**

42. **(Canceled)**

43. **(Original)** A method of changing a target sequence in genomic DNA of a mammalian cell, comprising:
(a) introducing a chimeric nuclease, or nucleic acid encoding the chimeric nucleic acid, into the cell, wherein said chimeric nuclease comprises: (i) a DNA binding domain; and (ii) a cleavage domain; and
(b) introducing a repair substrate into the cell, wherein said repair substrate comprises: (i) a nucleic acid sequence that is substantially identical to a region surrounding the target sequence; and (ii) a nucleic acid sequence which changes the target sequence upon recombination between the repair substrate and the target sequence,
whereby the target sequence is changed by the repair substrate upon recombination.

44.-64. **(Canceled)**

65. **(Original)** A method for ameliorating, treating or preventing, in an individual in need thereof, a disease caused, in part or in whole, by a genomic target sequence, the method comprising:
(a) introducing a chimeric nuclease into a cell, wherein said chimeric nuclease comprises: (i) a DNA binding domain; and (ii) a cleavage domain; and
(b) introducing a repair substrate into the cell, wherein said repair substrate comprises: (i) a nucleic acid sequence that is substantially identical to a region flanking the target sequence in chromosomal DNA; and (ii) a nucleic acid sequence which replaces the target sequence upon recombination between the repair substrate and the target sequence,
whereby the target sequence is altered in the cell, and the disease is ameliorated, treated or prevented.

66.- 89. **(Canceled)**

90. **(Original)** A method of designing a nucleic acid encoding a chimeric nuclease, comprising:
(a) selecting a mammalian target sequence for gene targeting;
(b) identifying a possible DNA binding sequence within workable proximity of the target sequence;

(c) designing a nucleic acid encoding a DNA binding domain that binds to the DNA binding sequence identified in (b); and

(d) coupling the nucleic acid encoding the DNA binding domain in (c) to a nucleic acid encoding a cleavage domain to make a nucleic acid comprising the coding sequence for the chimeric nuclease.

91.- 97. **(Canceled)**